

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P03-0030PCT		FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2004/004190	International filing date (day/month/year) 25.03.2004	Priority date (day/month/year) 26.03.2003	
International Patent Classification (IPC) or national classification and IPC			
Applicant PHARMADESIGN, INC.			

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>6</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (sent to the applicant and to the International Bureau) a total of <u>4</u> sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input checked="" type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s))</p> <p><u>1 flexible disk</u>, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																									
<p>4. This report contains indications relating to the following items:</p> <table border="0"> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/004190

Box No. I

Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☐ the international application as originally filed/furnished
- ☒ the description:
- pages 1, 2, 5-23 as originally filed/furnished
- pages* 3, 3/1, 4 received by this Authority on 26.01.2005
- pages* _____ received by this Authority on _____
- ☒ the claims:
- nos. 7-10 as originally filed/furnished
- nos.* _____ as amended (together with any statement) under Article 19
- nos.* 1-6 received by this Authority on 26.01.2005
- nos.* _____ received by this Authority on _____
- ☒ the drawings:
- sheets 1/11-11/11 as originally filed/furnished
- sheets* _____ received by this Authority on _____
- sheets* _____ received by this Authority on _____
- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/004190

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement					
1. Statement						
Novelty (N)	Claims	1-10	YES			
	Claims		NO			
Inventive step (IS)	Claims	1-10	YES			
	Claims		NO			
Industrial applicability (IA)	Claims	1-10	YES			
	Claims		NO			
2. Citations and explanations (Rule 70.7)						
Document 1: The Journal of General Physiology, Vol. 115, No. 5, 2000, pages 583 to 598						
Document 2: WO 01/76618 A1 (Univ. New York State Res. Found.), 18 October 2001						
Document 3: Nature, Vol. 409, No. 6816, 2001, pages 35 to 36						
The invention that is set forth in claims 1 to 10 is not disclosed in any of documents 1 to 3, which are cited in the international search report; therefore, the invention in question is novel and involves an inventive step.						

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. Claim 3

The polypeptides (or salts thereof) that are set forth in claim 3 are characterized in that: they comprise an "amino acid sequence that is configured by deleting, substituting inserting or adding one or a plurality of amino acids" within the amino acid sequences that are represented by SEQ ID NO: 1 and SEQ ID NO: 2; they form intramolecular disulfide bonds; and they exhibit an activity whereby they inhibit mechano-sensitive channels.

Therein, the number of amino acids within the amino acid sequences that are represented by SEQ ID NO: 1 and SEQ ID NO: 2 are as follows: the amino acid sequence that is represented by SEQ ID NO: 1 comprises 10 amino acids, and the amino acid sequence that is represented by SEQ ID NO: 2 comprises 8 amino acids. Therefore, deleting amino acids at arbitrary positions, substituting amino acids at arbitrary positions with an arbitrary amino acid from among the approximately 20 types of existing amino acids, or inserting and/or adding (an) arbitrary amino acid(s) at arbitrary positions within these amino acid sequences will give a large number of amino acid sequences that have a structure which is capable of forming intramolecular disulfide bonds, regardless of whether or not these amino acid sequences exhibit an activity whereby they inhibit mechano-sensitive channels (ultimately, since it is sufficient that an intramolecular disulfide bond be formed, the Cys molecules within SEQ ID NO: 1 or 2 can be substituted freely as long as there are two Cys molecules at arbitrary positions so that in the end an intramolecular

Box No. VIII Certain observations on the international application

disulfide bond will be formed).

Consequently, it is thought that a person skilled in the art would have to carry out a excessive amount of screening and experimentation in order to select the amino acid sequences that exhibit an activity whereby they inhibit mechano-sensitive channels from among this large number of amino acid sequences, even with consideration of common technical knowledge at the time the present application was filed.

As a result, the detailed description of the present invention cannot be considered to be disclosed in a manner that is sufficiently clear and complete for the invention that is set forth in claim 3 to be carried out by a person skilled in the art.

2. Claims 9 and 10

The inventions set forth in claims 9 and 10 include inhibitors or therapeutic agents which comprise the polypeptides that are set forth in claim 3.

Consequently, due to the fact that the polypeptides that are set forth in claim 3 suffer from the defects that are indicated in section 1, above, the inventions set forth in claims 9 and 10, which include inhibitors or therapeutic agents that comprise the polypeptides that are set forth in claim 3, will also suffer from the same defects as are indicated above.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/004190

Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment* on _____
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."